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New Drug Treatment Possibilities for Alzheimer's

UC Santa Barbara scientists have made a discovery that has the potential for use in the early diagnosis and eventual treatment of plaque-related diseases such as Alzheimer's disease and Type 2 diabetes.

The amyloid diseases are characterized by plaque that aggregates into toxic agents that interact with cellular machinery, explained Michael T. Bowers, lead author and professor in the Department of Chemistry and Biochemistry. Other amyloid diseases include Parkinson's disease, Huntington's disease, and atherosclerosis. Amyloid plaques are protein fibrils that, in the case of Alzheimer's disease, develop prior to the appearance of symptoms.

"The systems we use are model systems, but the results are groundbreaking," said Bowers. He explained that his research provides the first examples of the conversion of randomly assembled aggregates of small peptides into ordered beta sheets that comprise fibrils. Fibrils are the final structural state of the aggregation process.

Their work is published in a recent issue of Nature Chemistry. In the article, Bowers describes how understanding the fundamental forces that relate aggregation, shape, and biochemistry of soluble peptide aggregates is central to developing diagnostic and therapeutic strategies for amyloid diseases.

Bowers and his research team used a method called Ion-mobility Spectrometry-mass Spectrometry (IMS-MS). This method enabled the team to deduce the peptide self-assembly method. They then examined a series of amyloid-forming peptides clipped from larger peptides or proteins associated with disease.

Bowers explained that IMS-MS has the potential to open new avenues for investigating the pathogenic mechanisms of amyloid diseases, their early diagnosis and eventual treatment.

The first author of the paper is Christian Blieholder, a Humbolt Postdoctoral Fellow at UCSB. Thomas Wytttenbach, UCSB associate researcher, is a co-author. Nicholas F. Dupuis, who was a Ph.D. student at UCSB at the time of the research, is also a co-author; he is now a postdoctoral fellow at the University of Colorado.

Source: Christian Blieholder, Nicholas F. Dupuis, Thomas Wytttenbach, Michael T. Bowers. Ion mobility-mass spectrometry reveals a conformational conversion from random assembly to β -sheet in amyloid fibril formation. Nature Chemistry, 2010; 3 (2): 172 DOI: 10.1038/nchem.945